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PATENT APPLICATION

31st July 1973

Director-General, Japanese Patent Office

1. Title of the Invention

   A method for the production of tetrahydro-isoquinoline derivatives

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(19) Japanese Patent Office

The Laid-Open Patent Gazette

(11)	Publication number	50-35175 (35175-1975)
(43)	Publication date	3rd April 1975
(21)	Application number	48-86072 (86072-1973)
(22)	Application date	31st July 1973
Request for examination		Not received
(Total number of sheets)		Seven

Office File Nos.

6855 44
7043 44

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(52) Japanese Class.	(51) Int.Cl^2
16 E433	C07D 217/02//
30 B4	A61K 31/47

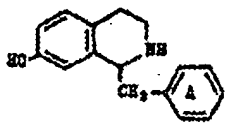
Specification

Title of the Invention

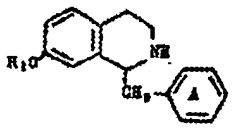
A method for the production of tetrahydroisoquinoline derivatives

Scope of Claim

A method for the production of tetrahydroisoquinoline derivatives represented by the general formula



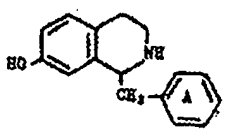
(where, ring A represents a phenyl group substituted with three lower alkoxy groups), which is characterized in that the 7-acyloxy-1-benzyl-1,2,3,4-tetrahydro-isoquinoline derivatives represented by the general formula



(where R_1 represents an organic acyl group and A has the same meaning as above) are subjected to hydrolysis.

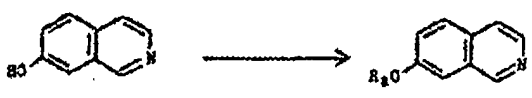
Detailed Description of the Invention

The present invention relates to a method for the production of the novel tetrahydroisoquinoline derivatives represented by general formula

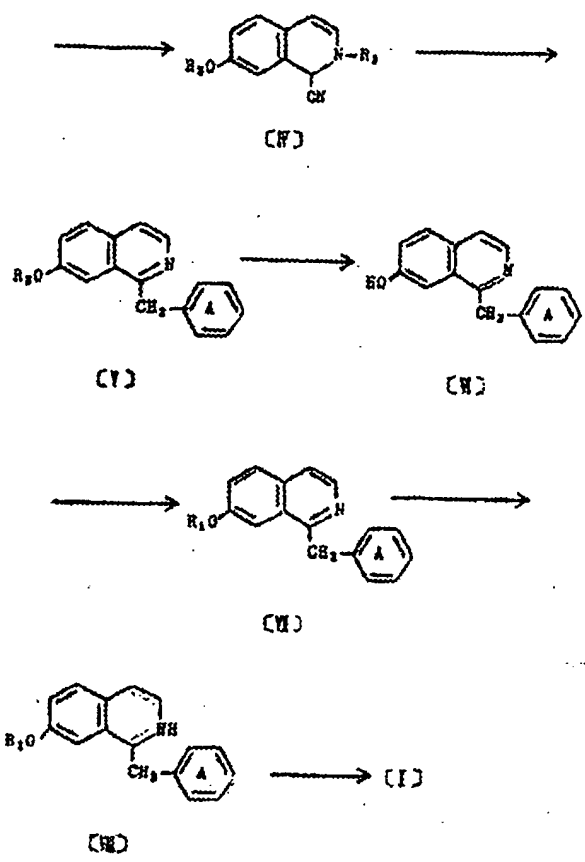
 (I)

(where, ring A represents a phenyl group substituted with three lower alkoxy groups).

It is already known from, for example, West German Laid-Open Patent Publication No. 2162563 and Japanese Patent Publication No. 48-7114 that 6-hydroxy-1-trimethoxybenzyl-1,2,3,4-tetrahydroisoquinoline and the like are useful compounds which have a vasodilating action. However, while the production of these compounds having a hydroxy group at the 6-position on the 1,2,3,4-tetrahydroisoquinoline skeletal structure is comparatively easy, the production of compounds with a hydroxy group only at the 7-position is not easy. As a result of research, the present inventors have succeeded in producing various compounds with the hydroxy group only at the 7-position and, furthermore, they have discovered that amongst these compounds the 1,2,3,4-tetrahydroisoquinoline derivatives [I] which have a trialkoxybenzyl group at the 1-position have a markedly more powerful blood flow increasing action than the aforesaid known compounds. For example, when compared to the corresponding 6-hydroxy compound, 7-hydroxy-1-(3,4,5-trimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (hydrochloride) has at least a 10 times more powerful blood flow increasing action in the common carotid artery of the dog. In accordance with the present invention, the compounds [I] can be produced by the method represented by the following reaction scheme.



〔II〕 〔III〕



(Here, R_1 and R_3 represent the same or different organic acyl groups and R_2 is an aralkyl group. Ring A has the same meaning as above.)